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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/886,964	06/21/2001	Ya Fang Liu	YFLU-P02-001	6742
23628	7590	06/29/2006	EXAMINER	
WOLF GREENFIELD & SACKS, PC FEDERAL RESERVE PLAZA 600 ATLANTIC AVENUE BOSTON, MA 02210-2206				KOSAR, ANDREW D
ART UNIT		PAPER NUMBER		
		1654		

DATE MAILED: 06/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/886,964	LIU, YA FANG
	Examiner Andrew D. Kosar	Art Unit 1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 26 April 2006.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 36,39,40 and 44-48 is/are pending in the application.
- 4a) Of the above claim(s) 45-48 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 36,39,40 and 44 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                    | Paper No(s)/Mail Date: _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date: _____ | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|   | 6) <input type="checkbox"/> Other: _____                                    |

## DETAILED ACTION

### *Response to Amendment/Arguments*

Applicant's arguments and amendments filed April 26, 2006 are acknowledged and have been fully considered.

#### The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**Claims 36, 39, 40 and 44** are rejected/remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for the reasons of record and those set forth below. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. Please note, the new limitation in the claim does not alter the rejection of record.

Applicant argues that the amendment to the claims of November 19, 2004, amending the claims to recite, "that blocks ATP binding to MLK by binding to a MLK ATP binding site" is not new matter because allegedly Example 3 in conjunction with, "the disclosure in the application of MLK inhibitors as compounds that inhibit MLK protein activity, e.g. a kinase activity (see, e.g., page 12, lines 22-24 and page 21, lines 18-21), is sufficient to indicate to the skilled person that Applicant was in possession of the invention as claimed." (page 9, New Matter, 2<sup>nd</sup> paragraph).

MPEP § 2163 states that, "[n]ew or amended claims which introduce elements or limitations which are not supported by the as-filed disclosure violate the written description

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requirement. See, e.g., *In re Lukach*, 442 F.2d 967, 169 USPQ 795 (CCPA 1971) (subgenus range was not supported by generic disclosure and specific example within the subgenus range); *In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972) (a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads).” Further, the MPEP states, “[w]hile there is no *in haec verba* requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure.”

In the instant case, the introduction of the limitation of the MLK inhibitor being one that “blocks ATP binding to MLK by binding to a MLK ATP binding site,” amended the scope of the claims from inhibiting, “any measurable biochemical activity possessed by the protein” (*Specification* page 12, line 23-24) to a specific biological process and mechanism (inhibits ATP binding by binding to the ATP binding site) which lacks explicit, implicit or inherent disclosure. The definition of MLK activity in the specification is, “any measurable biochemical activity possessed by the protein, e.g. a kinase activity or an ability to bind to another protein such as c-Jun,” which fails to provide express, implicit or inherent disclosure to support the amendment.

Further, Applicant asserts that the amendment to the claim is supported by the mutation of the ATP binding site. Mutation of the ATP binding site is significantly different than an inhibitor that binds in the ATP binding site, and puts Applicant in possession of a mutated binding site, and not an inhibitor of the native protein, and thus alone or in combination, the specification fails to provide express, implicit or inherent disclosure to overcome the rejection.

Thus, for the reasons of record, and those set forth above, the rejection is maintained.

**Claims 36, 39, 40 and 44** remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, for the reasons of record and those set forth below.

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The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant has amended the scope of the claims to now encompass “reduces and/or prevents” neuronal cell death. The introduction of this limitation does not alter the rejection of record.

Applicant argues that the compounds usable in the method, “could be determined by one of ordinary skill in the art based on the structural constraints imposed by the protein structure,” (page 4, Breadth of the claims) and that kinase inhibitors that bind to ATP binding domains are known in the art (page 7, 3<sup>rd</sup> paragraph).

As stated in the previous Office Actions, Applicant has not provided a single compound used, or obtained by screening, in the instantly claimed method. Alleging that the compounds usable are those that bind to the ATP binding site adds the complexity to the already burdensome method of determining where the compound binds. Furthermore, as stated previously, Applicant has not disclosed a single compound that would be usable in treating Parkinson’s disease, working or prophetic.

Applicant further argues that the mutant MLK, “can be viewed as an equivalent of MLK inactivated by inhibitor binding.” (page 7, lines 2-4). This is simply not the case. One would not reasonable extrapolate a mutant protein equates to possession of an inhibitor of an enzyme, and Applicant has not provided any evidence to support such an assertion.

Furthermore, Applicant states quite the contrary, “It is true that this molecule [the mutant enzyme], by itself, is not a teaching of an inhibitor molecule that binds to the ATP binding site of

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MLK.” (page 7, lines 4-5). Again, Applicant asserts, without any supporting evidence, that one of skill in the art would understand the correlation.

With regards to the unpredictability in the animal model, Applicant asserts that the Examiner must provide references that rebut the assertion that animal models of Parkinson’s, “known to one of ordinary skill in the art were both relevant and reasonable for extrapolation to human disease,” (page 8, last paragraph), further stating that, “Applicant knows of no evidence that the skilled person would have believed anything other”. Respectfully, the Examiner has clearly set forth that the model was recognized by the art to be both unpredictable and even questioned the validity of the model (e.g. Non-Final Rejection of October 21, 2005, pages 7-10). Certainly, such unpredictability indicates that the model is neither relevant nor reasonable for extrapolation to human disease.

Thus, for the reasons of record, and those set forth above, the rejection is maintained that it would be an undue burden to practice the method commensurate with the claims.

**Claims 36, 39, 40 and 44** are rejected/remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for the reasons of record and those set forth below. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection. Please note, the new limitation in the claim does not alter the rejection of record.

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Applicant argues that the written description is satisfied and that partial structure has been provided. Applicant asserts that the knowledge of the binding site of the MLK is sufficient to describe the genus of inhibitors of MLK activity (page 10, last paragraph).

The examiner disagrees. Description of a binding pocket provides no information regarding an inhibitor that works in the method as claimed, and Applicant has provided no evidence to support such an assertion.

Applicant further asserts that written description is an inverse relationship between level of skill/knowledge and disclosure. While the level of knowledge was high, Applicant misinterprets the Examiner's position, as the following statement is made in the Office Action of October 21, 2005, "As set forth under the enablement rejection the level of skill in the art is high. The knowledge in the art is such that no compounds were known that exhibited that activity." (emphasis added, page 16). Respectfully, it appears Applicant is misinterpreting the statement. When both sentences are taken together, and not parsed, as in Applicant's response, the level of skill in the art could be considered very low, as no compounds are/were known to have the desired activity in the method. Indicating that the level of skill/knowledge is 'high' is an indication that the art clearly recognized that no compounds were known to function as instantly claimed. Applicant has failed to disclose a single species, let alone a sufficient variety of compounds, that would work in the instant method, to describe the genus of 'inhibitors' adequately, and thus for the reasons of record, and those set forth above, the rejection is maintained.

### **Conclusion**

**NO CLAIMS ARE ALLOWED.**

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**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

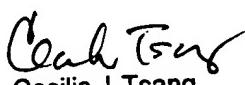
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

This application contains claims 45-48 drawn to an invention nonelected with traverse in the reply filed February 3, 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 8am-430pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
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